I. Status of the Claims

By the foregoing amendments, claims 1, 2, 6-9, 16 and 17 have been amended and non-elected claims 10-15 have been cancelled. Upon entry of the foregoing amendments claims 1-4, 6-9, and 16-20 are pending in the present application.

II. The Objection to the Specification

In the Office Action at pages 2 and 3, the Examiner has maintained the objected to the specification because it allegedly contains embedded hyperlinks and/or other forms of browser executable code. Applicants submit that the prior amendment, accompanying the response submitted December 21, 2001, which removed the text "http://" from the uniform resource locators (URLs) was sufficient to overcome the Examiner's objection. Although Applicants believe the previous amendment placed the specification in compliance with MPEP 608.01, in order to accommodated the Examiner's further objection Applicants have amended the of the specification to remove "www." prefixes and to indicate that the URLs may be found on the world wide web. No new matter was added by way of this amendment.

III. Rejection Under 35 U.S.C. § 101

In the Office Action at pages 3 and 4, the Examiner has maintained the rejection of claims 1-4, 6-9, and 16-20 under 35 U.S.C. § 101, as lacking a patentable utility due to an alleged failure of the claimed invention to be supported by a specific, substantial, and credible utility, or in the alternative, a well established utility. Applicants respectfully traverse this rejection.

Claims 1-4, 6-9, and 16-20 were rejected under 35 U.S.C. §101, as allegedly lacking utility. The Examiner contends that the utilities of the invention are not "specific" or "substantial" utilities. Office Action dated March 1, 2002 at page 3. Applicants respectfully disagree. It is well-established law that "when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983). The present specification describes many objectives that are met by the present invention including but not limited to determining the presence and/or identity of polymorphisms, measuring the levels of an mRNA in a sample, determining the location of a corresponding DNA sequence on a physical or genetic map, probing for other molecules, generating primers, obtaining other nucleic acid molecules from the same species, obtaining related protein coding sequences, obtaining promoters and other flanking genetic elements, screening cDNA genomic libraries, obtaining nucleic acid homologues, and detecting and characterizing gene expression. *See* the "Detailed Description of the Invention" beginning at page 17 including the section "(b) Protein and Peptide Molecules" and "Exemplary Uses of the Agents of the Invention," beginning on page 44

The Examiner maintains that the specification "does not teach any specific utilities for the claimed sequences." Office Action at page 3. However, Applicants maintain that the utilities are specific. For example, probing for a particular gene cannot be ascribed to any polynucleotide. Rather, a finite group of nucleotides is suited to this task. Thus, use of the claimed polynucleotides as probes enables identification of particular molecules. Accordingly, the use of the claimed polynucleotides as probes is specific.

The Examiner also contends that the utilities provided by the Applicants are not substantial "because further research needs to be done to determine any real world utility for obtaining the protein molecules, measuring the level of mRNA in a sample etc." Office Action dated March 1, 2002 at page 3. Applicants respectfully disagree. As the Supreme Court said in *Brenner v. Manson*, the "basic quid pro quo contemplated by the Constitution and the Congress for a patent monopoly is the benefit derived by the public from an invention with substantial utility ... where specific benefit exists in currently available form." 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Applicants have met their part of the bargain. They have provided nucleic acid molecules, that, in their current form, provide specific benefits to the public, such as, for example, detecting the presence or absence of polymophisms. These benefits are specific, not vague or unknown, and reflect a "real world," or substantial, benefit. Because the claimed nucleic acids provide at least this benefit, they satisfy the utility requirement of 35 U.S.C. § 101.

In fact, the utility standard has long been considered a *de minimis* one, seldom barring patentability. *Ex parte Drulard*, 223 U.S.P.Q. (BNA) 364 (PTO Bd. of Patent Appeals and Interferences 1983). The threshold for utility is not high: "An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). The utility requirement of Section 101 is merely shorthand for attributing real-world value to claimed subject matter. *Nelson v. Bowler & Crossley*, 626 F.2d 853, 856, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980). Accordingly, the courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip, Inc. v. Orange Bang,*

Inc., 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). For analytical purposes, the requirement for an "identifiable benefit" may be broken into two prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996).

The Examiner has provided no evidence that the claimed nucleic acid molecules will not work for the disclosed utilities. "[T]he initial burden of challenging a presumptively correct assertion of utility in the disclosure" falls upon the Examiner. *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q. 2d 1436, 1441 (Fed. Cir. 1995). Accordingly, the utilities disclosed by Applicants in the specification must be accepted as factually sound unless the Patent Office cites information that undermines the credibility of the assertion. *Id.* The Examiner "must do more than question operability – [he] must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975). In the Office Action, the Examiner provides no evidence supporting a challenge as to whether the claimed nucleic acid molecules would work for the disclosed utilities. In fact, the Examiner has admitted that the specification discloses the claimed nucleic acid molecules are operable for several asserted utilities. Office Action dated March 1, 2002 at page 5-6 and the Office Action dated September 25, 2001 at pages 8-9. Therefore, the Examiner has not met the requisite burden to impose a 35 U.S.C. § 101 rejection.

In view of the foregoing, Applicants submit that the claimed nucleic acid molecules are supported by specific and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any evidence challenging the presently asserted utilities. Consequently, the rejection of claim 1 under 35 U.S.C. § 101 is incorrect and should be withdrawn.

IV. Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

In the Office Action, at page 4, the Examiner has maintained the rejection of claim 1-4, 6-9, and 16-20 as not being enabled by the specification, because the claimed invention allegedly lacks utility. Applicants respectfully traverse this rejection. This rejection has been overcome by the foregoing arguments regarding utility. Thus, this rejection under 35 U.S.C. § 112, first paragraph is improper. Reconsideration and withdrawal are respectfully requested.

V. Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

The Examiner has maintained the rejection of claim 1-4, 6-9, and 16-20 under 35 U.S.C. § 112, first paragraph, for allegedly lacking an adequate written description "in the specification in such a way as to enable one skilled in the art to which it pertains, or to which it is most nearly connected, to make and/or use the invention". The Examiner asserts that Applicants' arguments, presented in the response dated December 21, 2001 were not persuasive, because

> there is substantial variability among the species of polynucleotides or nucleic acids encompassed within the scope of the claims because the claimed SEQ ID NO is only [a] fragment of any full-length gene or cDNA species, or any vector due to the use of open language 'comprising' or 'having.'

Office Action dated March 1, 2002 at page 5. Applicants respectfully traverse this rejection.

Applicants reiterate that they have provided detailed chemical structure of sequence of SEQ ID NO: 1 that distinguish the claimed molecules from other nucleic acid molecules. Response filed December 31, 2001, at page 12. The fact that the nucleic acid molecules may comprise additional sequences or variations is beside the point. Applicants have provided the nucleotide sequence required by the claims, *e.g.*, SEQ ID NO: 1, and have thus established possession of the claimed invention. The fact that the claims at issue are for example, intended to cover molecules that include the recited sequences joined with additional sequences does not mean that Applicants were any less in possession of the claimed nucleic acid molecules. Such modifications are readily envisioned by one of ordinary skill in the art, and disclosed through the present specification.

In addition to the foregoing, it is well-established that use of the transitional term "comprising" leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986). It is also well-established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques". *E.g.*, *Ajinomoto Co.*

v. Archer-Daniels-Midland Co., 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000).

In view of the foregoing reconsideration and withdrawal of this rejection is respectfully requested.

VI. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph (Enablement)

In the Office Action dated March 1, 2002, at page 5, the Examiner maintains the rejection of claims 1-4, 6-9, and 16-20 under 35 U.S.C. § 112, first paragraph for allegedly lacking enabling support commensurate with the scope of the claims. The Examiner alleges Applicants' arguments are not persuasive "because although the specification is enabling for nucleotides of the elected SEQ. ID NO: 1, it does not enable nucleic acids comprising or having the elected SEQ ID NO: 1 for the reasons set forth above" (*i.e.*, in the foregoing *35 U.S.C. § 112, First Paragraph* Written Description rejection).

Applicants respectfully traverse this rejection. While Examiner has acknowledged the election of SEQ ID NO: 1, and admitted the specification is enabling for nucleotides of elected SEQ ID NO: 1 at pages 8-9 of the September 25, 2001 Office Action, the Examiner subsequently asserted in the Office action dated March 1, 2002, that there is a lack of enablement within the scope of elected SEQ ID NO: 1. In view of the preceding, the finality of the March 2002 Office Action was premature as it set forth a new ground of rejection, and the finality of the Office Action should be withdrawn.

In addition to the foregoing, in order to sustain a rejection under 112 first paragraph for enablement, the Patent Office bears the burden of showing it would require undue experimentation by the public to make or use the claimed invention. In view of the Examiner's admission that SEQ ID NO: 1 is enabled, and the well-established patent

jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques" *E.g., Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000), which would include the use of the claimed sequence with other nucleic acid sequences, Applicants submit the Examiner has not met the required burden. Applicants further assert that the use of the transitional "comprising" or "having," which leaves the claims "open for the inclusion of unspecified ingredients even in major amounts" *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986) is well established in patent jurisprudence.

In view of the foregoing, reconsideration and withdrawal of this rejection is respectfully requested.

VII. Rejection of Claims Under 35 U.S.C. § 102(b)

Claims 1-2 and 17-18 are rejected under 35 U.S.C § 102(b) as being anticipated by Birren et al. (Genbank Accession No. AC005922)

In the Office Action at page 6, the Examiner has maintained the rejected claims 1-2 and 17-18 under 35 U.S.C. § 102(b), as allegedly being anticipated by a 22 nucleotide region of sequence disclosed by Birren *et al.* (Genbank accession No. AC005922, 11/14/98). Applicants respectfully traverse this rejection. Applicants have a priority claim to U.S. Application No. 60/163,469, filed November 1, 1999[1], which discloses the claimed

[1] Applicants note that response filed on December 21, 2001 indicated that support for SEQ ID NO: 1 could be found in United States Provisional Application No. 60/144,351. This was noted in error. Applicants note that support for SEQ ID NO. 1 can be found in United States Provisional Application No. 60/163,469, filed November 1, 1999.

sequence as SEQ ID NO: 17839. As the date relied upon by the Examiner in applying the Birren reference is less than one year prior to the date of filing of 60/163,469, the rejection under 35 U.S.C. § 102(b) is improper and should be withdrawn. Moreover, the Examiner has not established the date of public availability of the sequence in question. The date set forth on the reference could be the date of submission or entry into data base records not yet available to the public.

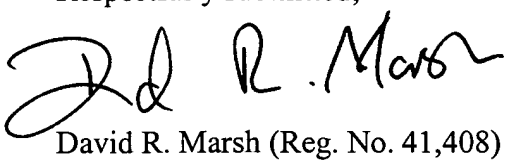
In addition to the foregoing, regardless of the date of availability the Birren reference does not anticipate Claim 1, as it does not disclose the sequence of SEQ ID NO: 1. In addition, Birren et al. cannot anticipate claims 17 and 18 as the sequence disclosed in the Birren reference does not have identity 90% or more of a nucleic acid molecule of SEQ ID NO: 1. Moreover, Birren et al. cannot anticipate claim 2 as it does not disclose a sequence from about 50 to about 100 nucleotides of SEQ ID NO: 1. In view of the foregoing, Applicants request reconsideration and withdrawal of this rejection.

VIII. Summary

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,



David R. Marsh (Reg. No. 41,408)
June E. Cohan (Reg. No. 43,741)

Date: June 3, 2002

Arnold and Porter
555 Twelfth Street
Washington, DC 20004-1206
(202) 942-5000 telephone
(202) 942-5999 facsimile

Marked-Up Version of the Amendments

In the Specification at page 3, line 21 through page 4, line 5:

Similarity analysis includes database search and alignment. Examples of public databases include those on the world wide web such as the DNA Database of Japan (DDBJ)([www.]at ddbj.nig.ac.jp/); [Genebank] Genbank ([www.] at ncbi.nlm.nih.gov/web/Genbank/Index.html); and the European Molecular Biology Laboratory Nucleic Acid Sequence Database (EMBL) ([www.] at ebi.ac.uk/ebi_docs/embl_db.html). A number of different search algorithms have been developed, one example of which are the suite of programs referred to as BLAST programs. There are five implementations of BLAST, three designed for nucleotide sequences queries (BLASTN, BLASTX, and TBLASTX) and two designed for protein sequence queries (BLASTP and TBLASTN) (Coulson, *Trends in Biotechnology, 12*:76-80 (1994); Birren, *et al.*, *Genome Analysis, 1*:543-559 (1997)).

In the Specification at page 8, lines 4-14:

A characteristic feature of a large scale shotgun sequencing project is that the sequence data can be processed and assembled into contiguous sequences (contigs), which represent a reconstruction of the original genome sequence from the cloned fragments. Likewise, individual Bacterial Artificial Chromosome (BAC) clones within a BAC library can be shot gun sequenced and these data can be assembled into contigs within each clone. Programs are available in the public domain that can analyze the sequence output and assemble the sequences into larger sequence regions representing contiguous sequences of the target genome. Examples of such programs can be found on the world wide web at, for example, genome.wustl.edu/gsc, [www.] sanger.ac.uk, and

[www.]mbt.washington.edu. An example of sequence reading program is Phred (found on the world wide web at [www.]mbt.washington.edu). Phred reads DNA sequencer trace data, calls bases, assigns quality values to the bases, and writes the base calls and quality values to output files.

In the Specification at page 8, line 15 through page 9, line 8:

The process of assembling DNA sequence fragments generally involves three phases; the overlap phase, the layout phase and the multi-alignment, or consensus, phase. In the overlap phase, each fragment is compared against every other fragment to determine if they share a common subsequence, an indication that they were potentially sampled from overlapping stretches of the original DNA strand. Pairs of fragments are compared in two ways; 1) with both fragments in the same relative orientation, and 2) with one of the fragments having been reverse complemented. In the layout phase, a series of alternate assemblies or layouts of the fragments based on the pairwise overlaps is generated. A layout specifies the relative locations and orientations of the fragments with respect to each other and is typically visualized as an arrangement of overlapping directed lines, one for each fragment. The general criterion for the layout phase is to produce plausible assemblies of maximum likelihood. In this manner, it can be determined if there is more than one way to put the pieces together and if different solutions appear equally plausible. In such a case, one would return to the lab and obtain additional information to resolve the ambiguity. The multi-alignment, or consensus, phase uses more information than just the pairwise alignments in the layout. The sequences of all the fragments in a layout are simultaneously aligned, giving a final set of contigs representing regions of the target

genome. An example of an assembly program is PHRAP, which can be found on the world wide web at [http://]chimera.biotech.washington.edu/UWGC/tools/phrap.htm.

In the claims

1. (Twice Amended) A substantially purified nucleic acid molecule having [a] the nucleic acid sequence of SEQ ID NO: 1 or the complement [complements] thereof.

17. (Twice Amended) A substantially purified nucleic acid molecule having between 90% and 100% sequence identity with [the second] a nucleic acid molecule having the sequence of SEQ ID NO: 1 or complements thereof.

18. (Once Amended) The substantially purified nucleic acid molecule of claim 17, wherein said substantially purified nucleic molecule has between 99% and 100% sequence identity with [said second nucleic acid molecule] a nucleic acid molecule having the sequence of SEQ ID NO: 1 or complements thereof.